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MEMORANDUM

February 18, 2000

SUBJECT: Response to Public Comments on the Preliminary Risk Assessment for the Organophosphate **Acephate**

FROM: Monica B. Alvarez, Chemical Review Manager
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TO: OPP Public Docket for Acephate

Introduction

This document addresses public comments that were received in response to EPA's Notice of Availability (64 FR 1199, January 8, 1999) of preliminary risk assessment for five organophosphate chemicals: acephate, disulfoton, methamidophos, oxydemethon methyl, and pirimiphos methyl. Each preliminary risk assessment may contain individual dietary (including drinking water), occupational, residential, and ecological assessments.

To better organize the comments in this document, EPA has divided this document into two parts. In addition, a subtitle or heading preceding the comments gives the reader a general idea of the subject discussed in a comment or group of comments. Part I of this document addresses comments specific to acephate. Comments specific to the acephate human health assessment were made by the registrant (Valent U.S.A. Corporation), the California Celery Research Advisory Board and the Scotts Company. Comments related to the environmental fate and ecological assessments were made by the Washington State Department of Agriculture, the Mint Industry Research Council and Valent U.S.A. Corporation.

Part II focuses on non-chemical-specific comments. Non-chemical-specific comments are those submitted to the OPP Public Dockets for each of the five chemicals or for a significant subset of the five. Also, these non-chemical-specific comments generally apply to regulatory or science policy issues that are not unique to any one of the risk assessments.

Full responses to some of the comments are outlined in a September 22, 1999 memorandum from Felecia Fort to Monica Alvarez and an August 25, 1999 memorandum from Stephanie Syslo and Michael Davy to Monica Alvarez. Both memoranda are contained in the OPP Public Docket for Acephate designated for Phase 5 of the TRAC process. In addition, detailed comments and responses on the occupational risk assessment assumptions and risk estimates can be found in the Agency's Revised Occupational and Non-Occupational Exposure and Risk Assessments for the RED Document (dated January 20, 2000). This document is also available in the OPP Public Docket for Acephate.

Note: Since the close of the public docket in March 1999, refinements have been made to both the Human Health and Ecological risk assessments for acephate. For further details on how these studies and refinements impacted the risk assessments, refer to the revised Human Health and Ecological risk assessments, which are now available in the Public Docket and on the Agency's website: www.epa.gov/pesticides/op/acephate.htm.

Part I: Acephate-Specific Comments and Responses

The Agency received acephate-specific comments from Valent U.S.A. (Valent or the registrant), the California Research Celery Board, the Washington State Department of Agriculture, the Mint Industry and the Scotts Company.

A. Response to Comments on the Preliminary Human Health Risk Assessment (HED chapter)

1. Comments from Valent U.S.A Corporation

Data Requirements on UV/Visible Absorption

Comment: Valent stated that the UV/VIS study will be conducted in 1999.

Response: The Agency has not yet received the UV/VIS study from Valent.

Data Requirements on Corrosion Characteristics

Comment: The requirement for corrosion characteristics should be waived because Orthene Technical is characterized as a dry powder (physical state). Valent commented that Orthene Technical is not corrosive as demonstrated by the lack of extreme pH of a 1% aqueous solution of the TGAI, pH 4.9. Packaging for the TGAI material for shipment and storage prior to formulating consists of an outer bag of polypropylene with a laminated five-ply polyethylene inner liner. Reaction between this inert polyethylene liner and the dry TGAI is unlikely.

Response: We consider the registrant's argument to be reasonable; however, a formal submission of the packaging material description is needed to support the registrant's statement and to justify waiving the requirements for corrosion characteristics.

75% FI Acephate Formulation

Comment: Valent elects not to support our 75% FI acephate formulation and will cancel this product registration.

Response: If the registrant cancels this product, no additional product chemistry data will be required for the 75% FI acephate formulation.

Certification of Suppliers

Comment: Valent submitted Product Chemistry Data to the Agency on September 17, 1998 and advised the Agency of our technical supplier. The Agency on January 21, 1999 advised Valent that our submitted product chemistry data have been reviewed and had been found to support our CSF and label.

Response: No additional data are required pertaining to the certification of suppliers of beginning materials and the manufacturing processes for the acephate manufacturing products.

Additional Field Trial Data

Comment: The Agency stated that additional field trial data and a processing study are required before the established tolerances for residues of acephate *per se* in/on soybeans may be reassessed. A processing study has been submitted. Valent believes the data requirement for aspirated grain fractions is not appropriate for acephate. In the submitted processing study, the data demonstrates no concentration of residues in meal, oil and hulls, therefore, no food/feed additive tolerance for the process fractions are required. The data demonstrate the soybean tolerance is sufficient for acephate residues in aspirated grain fractions (dust). Additionally, aspirated grain fractions should be viewed as a blended commodity. With Orthene's limited use on soybeans (<1% of total soybean acreage) acephate residues in blended grain elevator dust would be further reduced.

In the Agency's preliminary Residue Chemistry Chapter submitted to Valent on June 8, 1998, the Agency required data on cotton gin byproducts. Valent will conduct studies in 1999 to meet this requirement.

Response: EPA agrees with the registrant that additional residue data are not required for soybeans *per se*. The soybean processing study has been reviewed, and the results have been incorporated into the Revised Human Health Risk Assessment.

The Agency agrees with the registrant's rationale for waiving the requirements for soybean aspirated grain fraction residue study. Recently submitted soybean residue data (MRID No. 447770-02) validate the registrant claim that there are no concentration of acephate residues in soybean meal or hulls. Further percent crop treated (%CT) data indicated that the %CT is <1%. A soybean aspirated grain fraction study is no longer required.

Recommended Label Changes

Comment: Valent does not agree with the Agency's advisory to add a statement to our label which states that no methamidophos products should be applied after application of acephate since this may result in illegal residues. Valent has no knowledge of any illegal residues resulting from the use of acephate followed by methamidophos applications. Valent will conduct residue studies to support this position.

Response: The Agency has a continuing concern that use of both acephate and methamidophos in the same season, although unlikely, may result in illegal residues. Another option may be to amend labels to state that if both acephate and methamidophos are applied, the most restrictive PHI and seasonal application rate of the two labels should be used.

Acute and Chronic Dietary Risk Assessments Submitted by Valent

Comment: Valent stated that in its dietary assessment submitted to the Agency, acute and chronic dietary exposure and risk from both acephate and methamidophos (both as a metabolite from acephate and from direct use) are acceptable. Using data and data-handling assumptions acceptable to the Agency, anticipated residues, proportion of crop treated, etc., chronic exposures do not exceed 2.8 percent for acephate and 5.8 percent for methamidophos of their respective chronic reference doses. Tier 3 acute dietary exposure and risk analyses, using field residue and monitoring data, yield acceptable margins of exposure for both compounds (100 for acephate and 300 for methamidophos).

Valent stated that both acephate and methamidophos are analytes in the ARRI Market Basket Survey. More realistic residues in actual food will become available in the near future to further refine these analyses.

Response: EPA has reviewed the acute and chronic dietary exposure analyses submitted by the registrant, and the results have been addressed in a separate memorandum. Valent's Acute Probabilistic (Monte Carlo) Dietary Exposure Assessment (MRID #447746-02) is not acceptable due to consumption data, percent crop treated and hazard identification issues. However, considerable information in this submission (e.g., field trial data, processing factors) was included in the Agency's revised dietary exposure analysis.

The Agency's revised acute and chronic dietary analyses for acephate are highly refined. Although acephate dietary risks do not exceed the Agency's level of concern, acute dietary risk

from methamidophos from all sources (i.e., from the application of methamidophos and from the application of acephate) exceeds the Agency's level of concern.

Acute Oral LD_{50}

Comment: The registrant, Valent U.S.A. commented that the acute oral LD_{50} cited in Table 1 of the Science Assessment Section of the Human Health Risk Assessment for acephate technical was incorrect and that acephate technical should be classified as Category III.

Response: The Agency notes this error and has corrected the Table as follows and has incorporated the correct information into the Revised Toxicology Chapter and the Revised Human Health Risk Assessment.

Guideline No.	Result	Toxicity Category
Acute Oral Rat LD_{50} (Rat) MRID No.00014675	945 mg/kg ♂ 866 mg/kg ♀	3
Acute Oral Rat LD_{50} Recalculation (Rat) MRID No. 00029696	1.4 g/kg ♂ 1.0 g/kg ♀	3

Eye Irritation

Comment: The registrant also noted that acephate technical should be listed as a Category IV eye irritant rather than Category II, based on two eye irritation studies.

Response: The Agency agrees with the registrant and has incorporated this change into the Revised Toxicology Chapter and the Revised Human Health Risk Assessment to indicate a Toxicity Category of IV. Based on our re-evaluation of the primary eye irritation study (MRID No. 00014686) cited in the Toxicology Chapter for acephate technical, the conjunctival redness and discharge present in one rabbit on day 7 was graded a score of 1 according to the Draize scoring system for irritation.

Request to Include the NOEL Derived from the 90-day Feeding Study in the Revised Toxicology Chapter

Comment: The registrant requested that the Agency incorporate the conclusion stated in the 1998 Hazard Identification Committee's report that 2 ppm is the NOEL for the 90-day Feeding Study with Acephate: Special Cholinesterase study.

Response: The comment has been noted for this study (MRID No. 40504819), and the change has been incorporated into the Revised Toxicology Chapter and the Revised Human Health Risk Assessment.

NOEL for the Inhalation Studies is Underestimated

Comment: The registrant commented that the NOEL for the two subchronic inhalation studies with acephate is an underestimate of the actual NOEL, because the study was conducted with whole-body exposure conditions and that it is recognized and even verified in these studies that a whole-body exposure study results in dermal and oral exposures in addition to the inhalation exposure.

Response: The Agency is aware that the two subchronic studies (MRID Nos. 40504818 and 40645903) used whole-body exposures and agrees that an animal's total exposure is greater in a whole-body chamber than for nose-only exposures. However, the Agency has no policy on this issue and there is no precedent for making an adjustment to correct for the oral and dermal exposure routes. As stated in the Inhalation Risk Characterization and the Aggregate Risk Index (ARI) Memorandum from J. E. Whalen and H.M. Pettigrew to M. Stasikowski, dated November 25, 1998, "Although whole-body data overstate the risk, the error is in the direction of safety."

It should, nevertheless, be noted that in both of the above studies, animals were rinsed in tepid tap water after exposure to reduce topical exposure to Acephate.

Request to Include the 21-day Dermal Toxicity Study in the Human Health Risk Assessment

Comment: The registrant requested that a paragraph discussing the results of the 21-day dermal toxicity study (MRID No. 44541101) be added to the HED Risk Assessment Document.

Response: At the time the Hazard Identification Assessment Review Committee (HIARC) convened on December 11, 1997, only a draft copy of the report of the 21-day dermal toxicity in rats with Acephate Technical was available. This study was not formally submitted to the Agency until March 12, 1999, therefore, was not formally reviewed until after the Toxicology Chapter of the Human Health Risk Assessment was prepared. However, the results from this study were used at the HIARC meeting, December 11, 1997, to select the doses and toxicology endpoints for the short-term and intermediate-term dermal exposure scenarios (see HED Document No. 012453). Since that time, the study has received a formal review, and the summary has been incorporated into the Revised Toxicology Chapter and the Revised Human Health Risk Assessment (Also see Memorandum: N.E. MCCarroll, to P. Wagner, J. Rowland, F. Fort and L. Phan, dated May 26, 1999; HED Document No. 013396).

Request to Consider Pilot and Main 21-day Dermal Studies

Comment: The registrant requested the Agency to consider both the main study as well as the data from the pilot study for the 21-day dermal study for the dermal exposure scenarios.

Response: As part of the review of the submitted study, both the pilot and main study (MRID No. 44541101) were evaluated, and findings from both phases of testing were included in the Data Evaluation Record (DER). Based on the review, EPA concluded that the effects at 60 mg/kg/day were valid in the main 21-day dermal study because cholinesterase inhibition (ChEI) occurred in a dose-related manner, was significant and ChE activity was seen in the brain. The systemic LOAEL was, therefore, set at 60 ppm; the NOAEL was 12 mg/kg/day. By contrast, the pattern of brain ChEI in the 5-day dermal pilot was not clearly evident because of the variability in the data at 50 and 150 mg/kg/day (i.e., standard deviations were in excess [≈2.5x] of the standard deviations for the other groups [0.64-0/79] and in all groups in the main study [0.55-0.83]. Based on these considerations, the NOAEL and LOAEL (12 and 60 mg/kg/day, respectively) selected by the HIARC for the short-term and intermediate-term dermal exposure scenarios (see HED Document No. 012453) remain unchanged.

Request to Add Results from Pilot Neurotoxicity Studies to the Human Health Risk Assessment

Comment: The registrant requested that a paragraph discussing the results of the two pilot acute neurotoxicity studies be added to the HED Risk Assessment Document.

Response: Both of these acute range-finding neurotoxicity studies in rats (MRID Nos. 44203301 and 44203302) were reviewed and included in the DER prepared for the main study (MRID No. 44203303) (see HED Document No. 012416). Summaries have been extracted from the DER and have been incorporated into the revised Toxicology Chapter and the Revised Human Health Risk Assessment.

2. Comments from the California Celery Research Advisory Board (CCRAB)

Conservativeness of the Agency's Preliminary Dietary Risk Assessment

Comment: CCRAB stated that EPA's conservative assumptions, used in calculating the potential dietary exposure, indicated overexposures with the current uses of acephate. The CCRAB believes that the use of realistic data along with a more refined risk assessment would produce a more accurate estimate of exposure and in turn allow for better decisions to reduce overexposures that may be present. EPA's acute risk assessment assumes that all the crops are treated at the maximum label rates and that 100% of the crop is treated. EPA has tried to account for percent crop treated in the chronic dietary risk assessment; however, the Agency did not provide any of the data used in the risk assessment on percent crop treated. Such information should be included for comment. Additionally, the use of tolerance level residues substantially contributes to the calculation of overexposure.

Response: The preliminary risk assessment was a Tier1 acute dietary assessment using worst-case estimates, i.e. tolerance level residues and no percent crop treated data. A more refined probabilistic acute assessment which incorporates percent crop treated and anticipated residues has been conducted and is included in the revised Human Health Risk Assessment.

3. Comments from the Scotts Company

Body Burden Based on Inhalation Exposure

Comment: Dr. J. Ford, Scotts Company commented that the inhalation dose in the whole-body inhalation study becomes exaggerated since the EPA assessment assumes that the entire Acephate body burden was due to inhalation exposure.

Response: The Agency is aware that the two subchronic studies (MRID Nos. 4054818 and 40645903) used whole-body exposures and agrees that an animal's total exposure is greater in a whole-body chamber than for nose-only exposures. However, the Agency has no policy on this issue and there is no precedent for making an adjustment to correct for the oral and dermal exposure routes. As stated in the Inhalation Risk Characterization and the Aggregate Risk Index (ARI) Memorandum from J. E. Whalen and H.M. Pettigrew to M. Stasikowski, dated November 25, 1998, "Although whole-body data overstate the risk, the error is in the direction of safety."

It should, nevertheless, be noted that in both of the above studies, animals were rinsed in tepid tap water after exposure to reduce topical exposure to Acephate.

Dermal NOAEL

Comment: Dr. J. Ford, Scotts Company disagreed with the NOAEL set by EPA for the 21-day dermal study in rats and recalculated the dermal risk values based on a dermal NOAEL of 50 mg/kg/day from the 5-day pilot dermal study.

Response: As part of the review of the submitted study, both the pilot and main study (MRID No. 44541101) were evaluated and findings from both phases of testing were included in the Data Evaluation Record (DER). Based on the review, it was concluded by EPA reviewers and the expert dermal toxicologist member of the HIARC that the effects at 60 mg/kg/day were valid in the main 21-day dermal study because cholinesterase inhibition (ChEI) occurred in a dose-related manner, was significant and ChE activity was seen in the brain. The systemic LOAEL was, therefore, set at 60 ppm; the NOAEL was 12 mg/kg/day. By contrast, the pattern of brain ChEI in the 5-day dermal pilot was not clearly evident because of the variability in the data at 50 and 150 mg/kg/day (i.e., standard deviations were in excess [≈2.5x] of the standard deviations for the other groups [0.64-0/79] and in all groups in the main study [0.55-0.83]. Based on these considerations, the NOAEL and LOAEL (12 and 60 mg/kg/day, respectively) selected by the HIARC for the short-term and intermediate-term dermal exposure scenarios (see HED Document No. 012453) remain unchanged.

Occupational Risk Assessment Assumptions

Comment: The Scotts Company also submitted detailed comments on the occupational risk assessment assumptions and risk estimates.

Response: The Agency's responses can be found in the Revised Occupational and Non-Occupational Exposure and Risk Assessments for the RED Document (dated January 20, 2000). This document is available in the OPP Public Docket for Acephate.

B. Response to Comments on the Preliminary Ecological Risk Assessment (EFED chapter)

1. Comments from the Washington State Department of Agriculture

Toxicity to Bees

Comment: Mr. Johansen comments that "acephate is hazardous to honey bees, alkali bees and alfalfa leaf-cutting bees for 3 days when applied to blooming crops or weeds." Washington State University/Department of Agriculture investigated approximately 135 bee kills from 1992 to 1998. In several cases, acephate was responsible for killing honey bees when it was applied to blooming mint. Mr. Johansen strongly recommends that EPA require acephate labels to specifically warn applicators about the hazard of killing bees when making applications to blooming mint.

Mr. Johansen submitted computerized records on the bee incidents in 1993. These records show that there were 7 incidents in Washington State in which bee colonies were adversely impacted from the use of acephate on nearby mint and carrot fields. Acephate residues on bees were detected in all of these incidents in concentrations up to 2.63 ppm. Apiary losses range up to 60 hives per incident. These incidents will be recorded in the RED document.

Response: The Agency concurs with modifying the product labeling and would suggest the label language to be:

"This product is highly toxic to bees exposed to direct treatment on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds while bees are actively visiting the treatment area."

2. Comments from the Mint Industry Research Council

Benefits of Acephate Use on Mint

Comment: Rocky Lundy provided information on the use of acephate on mint and a testimonial to the benefits of retaining this use.

Response: The Agency will consider this information during the risk mitigation phase (Phase 5 of the TRAC Public Participation Process).

3. Comments from Valent U.S.A. Corporation

Environmental Fate and Transport Data

Abiotic Hydrolysis

Comment: Valent presented a synopsis of the study and indicated that material balances were acceptable and that "the experimental design did not allow for the capture and quantitation of volatile radioactivity."

Response: The Agency disagrees. At this time, the Agency has not received a formal response to the review of this study (MRID 41081604), and there are a number of comments in the DER in addition to the issue of material balance that remain to be addressed. Of particular interest is the difference in recovery of initial radioactivity between analytical methods. For the [S-methyl-^{14}C]acephate solutions at pH 9, the material balance based on LSC was 64.75%, while the material balance based on summing the amount of radioactivity identified during analysis by HPLC was 94.65%. While Valent states that "the experimental design did not allow for the capture and quantitation of volatile radioactivity", the Agency is aware of incubation and analytical methods that do allow for the capture and quantitation of volatile radioactivity. The registrant is encouraged to consult with the Agency on the study design before the study is repeated for [S-methyl-^{14}C]acephate at pH 9.

Photodegradation in Water

Comment: Valent cited the portion of the study conducted with a photosensitizer as a rationale for using a shorter half-life in the risk assessment.

Response: It is current Agency policy to use the photodegradation rate in the absence of a photosensitizer as an input for environmental modeling. In addition, since photolysis is not the major route of degradation for acephate (microbial metabolism is), the substitution of a half-life of 39.6 days will not qualitatively affect the predicted dissipation of acephate in the modeled scenarios. However, the effects of photosensitizers on the predicted chemical dissipation rates are considered during risk characterization.

Aerobic Soil Metabolism

Comment: Valent states that there are four unique soil degradates for acephate: RE-18420, aka O-methyl N-acetylphosphoramidate; RE-17246, aka O-methyl N-acetylphosphoramidothioate; DMPT, aka O,S-dimethyl phosphorothioate; and methamidophos, aka O,S-dimethyl phosphoramidothioate. They also state that "on average, about 10% of the applied acephate

degrades to methamidophos. In the worst case, only 23% of the applied acephate degrades to methamidophos. We have no data, generated by Valent or in the journal literature, to support instantaneous and quantitative environmental degradation of acephate to methamidophos."

Response: The Agency agrees that an instantaneous conversion to methamidophos from acephate is unlikely and that data are limited. However, the uncertainty as to the maximum concentration of methamidophos formed from acephate is high. In the revised Ecological Risk Assessment, the Agency uses a reduced conversion efficiency factor of 25%.

Aerobic Aquatic Metabolism

Comment: Valent proposes that for risk assessment purposes, the Agency should use an aerobic aquatic half-life of 4.5 days (3X the aerobic soil half-life).

Response: The Agency disagrees. Current Agency policy is that, if no acceptable aerobic aquatic metabolism data are available and the compound is stable to hydrolysis, the aerobic soil metabolism rate constant as determined from the 90% upper confidence bound of the mean half-life multiplied by a factor of 0.5, be used as a surrogate input for environmental modeling. However, in the absence of scientifically acceptable data, the uncertainty surrounding the EECs calculated using this surrogate information is high.

Mobility - Batch Equilibrium Studies

Comment: Valent stated that "Identification of soil by soil series name is not required by Guideline 163-1. The soils used in the study were characterized and USDA textural class reported." They also provided information on the percentage of organic matter contained in the clay loam soil used in the study.

Response: In the response to the methamidophos preliminary Ecological Risk Assessment, which also cited this study, Bayer provided information on the names of the soil series used. Using the information provided by Valent, percent organic matter is converted to percent organic carbon using the relationship % OM = 1.74 x % OC, which would result in a %OC of 1.9%. K_ds for acephate, methamidophos, and DMPT remain the same (0.09, 0.029, and 0.030 mL g^{-1}, respectively); the recalculated K_{oc}s are 4.7, 1.5, and 1.6 mL g^{-1}, respectively.

When taken together, the information individually provided by Bayer in their comments (soils identification) and Valent in theirs (percent organic matter) addresses the Agency's issues with this study. The study is now acceptable and can be used to fulfill the mobility data requirement for both acephate and methamidophos.

Accumulation - Bioaccumulation in Fish

Comment: Valent states that the bioconcentration factor may be less than the 10X reported.

Response: The Agency notes the comment, but can only use data derived from acceptable studies.

Field Dissipation

Comment: Valent disagrees with the Agency's rejection of a terrestrial field dissipation study (MRID 40504815; rejected because soil samples were not taken to an adequate depth to define leaching), and the registrant discusses this study in its comments.

Response: The Agency still considers the study to be unacceptable, because soil samples were not taken to an adequate depth to define leaching. The choice of a soil with a hardpan so close to the surface is not advisable, since, as noted by Valent, hardpan layers do restrict the downward movement of water. However, hardpan layers may be cracked or perforated, resulting in a continued downward movement of leaching water. As originally stated by the registrant, the study provided supplemental data on the field dissipation of acephate. These data are consistent with the results of the three acceptable field dissipation studies, and the terrestrial field dissipation data requirement is fulfilled.

Terrestrial Exposure Assessment

Comment: Valent believes that the use of short grass residue exposure is inappropriate.

Response: It is the Agency's policy to use the short grass exposure value from the Kenega/Fletcher nomogram. The highest exposure value from Kenega/Fletcher nomograph is 240 ppm on short grass for each pound of active ingredient that is sprayed on an acre. Although the Agency recognizes that most birds and mammals diet may not be 100% short grass, the Agency will use the short grass dietary exposure to reflect (as an index) exposure from inhalation, dermal and drinking water for wildlife. The Agency believes that this index would provide a more accurate and certain exposure value to reflect the toxicity of dermal, inhalation and drinking water exposures in lieu of available data. Should data be provided, the Agency will reconsider its exposure scenario.

Effect of Acephate Degradate Methamidophos on Birds and Mammals

Comment: Valent recommends adding the qualifying word "toxic" to language in this section regarding degradates of acephate.

Response: The Agency will change the language in this section to: "Therefore, it is likely that, following applications of acephate, the only toxic degradate of acephate that birds and mammals

will be exposed to is methamidophos."

Comment: Valent disagrees with the statement: "...it was assumed that, upon application of acephate, there would be an instantaneous and complete conversion to methamidophos." The registrant cites results of laboratory and field studies to counter this statement. The registrant also cites unidentified dislodgeable foliar residue studies regarding the amount of methamidophos present in leaf-punch wash solutions to demonstrate that "in plants, the assumption of instantaneous conversion results in a gross overestimation of exposure potential." The registrant also suggests replacing 77 % conversion factor for methamidophos formation from acephate applications with factors of 0, 25%, and 2% for water, soil, and plant applications, respectively.

Response: In the absence of data quantifying the rate of dissipation of acephate and the rate of formation and decline of acephate degradates on plant foliage following application, the Agency assumed a complete and instantaneous conversion of acephate to methamidophos for estimating terrestrial exposure to birds and mammals. It appears that, based on the data from the single acceptable aerobic soil metabolism study, the conversion is complete. (The aerobic soil metabolism half-life is often used by the Agency as a surrogate input for calculating the decline of pesticide residues on plant foliage when no foliar dissipation half-life value is available.)

The Agency agrees that an instantaneous conversion to methamidophos from acephate on plant foliage is unlikely. The results of dislodgeable foliar residues studies may not be appropriate for estimating the amount of total residue consumed by an animal if the pesticide is absorbed by the plant. Since acephate and methamidophos are considered to be systemic pesticides, residues absorbed by the leaves will not be removed by wash solutions. If the foliar dislodgeable studies also provide information of the <u>total</u> residues found in the leaf punches before washing, these studies may be helpful in estimating the exposure to wildlife from the consumption of plant materials at various times after foliar application of acephate.

Until those data are made available to the Agency for review, the Agency will not recalculate the RQs for birds and mammals due to the acephate degradate methamidophos. However, if one estimates the amounts of degradate residues on plant foliage from the results of the aerobic soil metabolism study using a conversion factor of 25% (rather than the 77% as was done in the preliminary Ecological Risk Assessment), this would not qualitatively affect the Ecological Risk Assessment (i.e., the acute RQs would remain above 1 for most uses, indicating high acute risk).

Surface Water Assessment

Surface Water EECs

Comment: Valent believes that the photosensitized half-life of 39.6 days for the aqueous photolysis input, the "default value of 3X the aerobic soil half-life" for the aerobic aquatic metabolism input, and the mean aerobic soil metabolism half-life of 1.5 days should be used in the

"GENEEC version 1.3" when calculating surface water EECs for acephate. They presented their generic estimated environmental concentrations (GEECs) based on those inputs.

Response: The Agency disagrees. As previously stated, it is current Agency policy to use the photodegradation rate in the absence of a photosensitizer and the aerobic soil metabolism rate constant, multiplied by a factor of 0.5 as inputs for environmental modeling. Current Agency guidance requires that the 90% upper confidence bound of the mean aerobic soil metabolism half-life (in this case, 2.3 days) be used as the soil half-life input. In addition, only GENEEC version 1.0 (executable dated 5/3/95) has been approved for use within the Agency. Using GENEEC version 1.0 and the inputs as stated in the Ecological Risk Assessment, with the exceptions of the default value for the aerobic aquatic metabolism input (2X 2.3 days, or 4.6 days) and the corrected K_{oc} (4.7 mL g^{-1}), the recalculated EECs are:

Table A. Generic EECs (in ppb) for Acephate for six applications of 1 lb/A to cotton

Application method	Peak GEEC	Average 4 Day GEEC	Average 21 Day GEEC	Average 56 Day GEEC
Aerial	94	77	31	12
Ground	93	75	30	12

The Ecological Risk Assessment has been corrected to reflect the changes to the inputs and GEECs noted above. Please note that the changes in the EECs do not qualitatively affect the conclusions of the assessment of the risk to nontarget aquatic animals, i.e., for most uses the LOC for endangered species of aquatic invertebrates are exceeded. There are no exceedances for acute risk, restricted use, or chronic risk.

Recalculated Methamidophos GEECs Based on a Conversion Rate of 25%

Comment: Valent also presented recalculated GEECs for methamidophos using an instantaneous conversion rate of 25%.

Response: The Agency agrees and has recalculated the GENEECs for methamidophos formed as a degradate of acephate using the 25% conversion factor (i.e., an "application rate" of 0.25 lb/A). Using GENEEC version 1.0 and the other inputs as stated in the Ecological Risk Assessment, with the exception of the corrected K_{oc} (1.5 mL g^{-1}), the recalculated EECs are:

Table A. Generic EECs (in ppb) for Methamidophos formed after six applications of 1 lb/A Acephate to cotton				
Application method	Peak GEEC	Average 4 Day GEEC	Average 21 Day GEEC	Average 56 Day GEEC
Aerial	22	22	18	12
Ground	21	20	16	11

The Ecological Risk Assessment has been corrected to reflect the changes to the inputs and GEECs noted above.

Drinking Water Assessment

Groundwater Concentration Estimates

Comment: Valent proposed using the recalculated SCI-GROW EEC for methamidophos using the 25% conversion factor (0.0037 μg/L).

Response: The Agency accepts the 25% conversion factor as an input for the Tier I screening models. The recalculated SCI-GROW EEC (taking into account the 25% conversion rate and the corrected K_{oc} of 1.5 mL g^{-1}) is 0.0047 μg/L). The Ecological Risk Assessment has been corrected to reflect the changes to the inputs and GEECs.

Surface Water Concentration Estimates

Comment: Valent believes that "EPA modelers chose the most conservative assumption, piling worst-case onto worst-case, resulting in unrealistic acephate EECs."

Response: The Agency disagrees. EPA's surface water modeling accounts for slope and soil properties assumed for vulnerable areas. The scenarios used in modeling are not a biased collection of high-end conservative combinations of site-related input parameter values. Instead, the model inputs are based on real world (actual site) interdependent combinations of slope, soil properties, crop, and application methods and scenarios. In addition, when Tier II modeling is triggered, variation in meteorological conditions is accounted for by use of time series of actual meteorological measurements. The plant foliage factors mentioned were set according to current Agency guidance on input selection. Because the inputs for PRZM were selected in accordance with previous Agency guidance, the peak concentrations for acephate in surface water did not change. However, using 0.5X the aerobic soil metabolism rate constant as the input for KBACW in EXAMS did affect the longer-term surface water concentrations of acephate. The PRZM-EXAMS simulations for acephate were rerun per previous guidance using the corrected value for KBACW and the new results were incorporated into the Revised Ecological Risk Assessment.

However, after the Ecological Risk Assessment was revised, the Agency established new guidance that incorporates the Index Reservoir (IR) and the Percent Crop Area (PCA) into the Agency's drinking water (from surface water) assessments. Recalculation of Tier II surface water EECs using this guidance will affect concentrations in some way, since cotton (the risk driver for surface water) is one of our IR scenarios with an established PCA.

The PRZM-EXAMS simulations for the degradate methamidophos will be removed from the Agency's Ecological Risk Assessment, because there is not sufficient information to appropriately use the algorithms included in PRZM to simulate the parent/daughter relationship. Because of the limited dataset for the formation and decline of methamidophos in soil following application of acephate, any estimate of the decay rate for acephate and the transformation rate of acephate to methamidophos needed for the PRZM simulation would have high uncertainty.

Ecological Effects Toxicity Assessment

Comment: Valent recommended that ecotoxicity endpoint be corrected as follows:

Chronic bird 5 ppm NOAEL be based on reduction in number of viable embryos, not mortality.

The lowest rainbow trout LC_{50} value is 110 ppm, not 730 ppm.

Chronic freshwater invertebrate daphnid NOAEC is based on reduction in the number of young, not mortality. The geometric mean of the NOAEC and LOAEC (MATC) is 0.237 ppm.

Response: EPA agrees with Valent concerning the chronic bird and the rainbow trout. The Agency also agrees with the registrant on the chronic NOAEC for daphnid being based on reduction in number of young and have changed these endpoints accordingly in the revised ecological risk assessment.

Birds, Chronic

Comment: Valent believes that literature references that are not directly related to acephate or methamidophos should not be included in the avian chronic toxicity section.

Response: EPA agrees with Valent, since the literature references are included in the exposure and risk assessment section of the document. Those references have been removed from the chronic toxicity section.

Estuarine and Marine Fish, Acute

Comment: Valent wants MRID 40228401 replaced with MRID 40098001 in the acute estuarine fish toxicity section since one is a duplicate.

Response: EPA notes that several MRID numbers are duplicates. The Agency has inserted MRID 40098001 in place of 40228401 to clear up confusion.

Toxicity to Plants

Comment: Valent will conduct Tier I vegetative vigor and seedling emergence studies with the end use product, ORTHENE® 75 S, instead of the active ingredient technical.

Response: EPA agrees with Valent.

Exposure and Risk Characterization

Comment: Valent notes that "exposure values and resultant risk characterization are for agricultural areas deliberately treated with acephate to control crop-destructive insect pests. Thus for exposure to occur, the bird, fish mammal, or insect must be either in the agricultural field or be feeding on crops sprayed for protection from harmful insects. These organisms are not captive and are free to move in or out of the treated area."

Response: The Agency assumes that wildlife are not aware of pesticide-danger and will be exposed to pesticide due to normal behavior patterns in which they have no reason to avoid treated areas. In addition, pesticides such as acephate do drift or runoff to non-target areas providing other areas for exposure.

Comment: Valent commented generally on the RQ tables.
"Terrestrial:

> "Concentrations of methamidophos derived from acephate are grossly over-estimated . . .
>
> "For acute exposure to both birds and mammals by acephate and (reduced) methamidophos, RQ values exceed level of concern only for the most intense exposure scenarios of small birds or mammals feeding exclusively on small grass from recently treated areas."

Response: The Agency has answered both of Valent's concerns in the Terrestrial Exposure section above.

Comment: "The endpoint used for chronic toxicity to birds is from an avian reproduction study with mallard ducks. The low endpoint combined with the high EEC values and slow dissipation leads to an expectation of high chronic risks. This risk is overstated because reproducing birds do not feed exclusively on food from treated areas."

Response: EPA maintains that several pesticides have been shown to reduce egg production within days after initiation of dietary exposure (Bennett et al 1991, Bennett and Bennett, 1991).

Effects of eggshell quality (Bennett and Bennett, 1990, Haegele and Tucker, 1974) and incubation and brood rearing behavior (Bennett et al, 1991, Brewer et al., 1988, Busby et al.,1990) have also resulted from short-term pesticide exposures. Therefore, for purposes of this risk assessment of acephate and methamidophos, the amount of time birds can be exposed to acephate or methamidophos after initial chemical exposure that will result in chronic effects can be as little as a day.

Comment: "For other examples of chronic exposure the RQ values exceeding levels of concern by acephate and (reduced) methamidophos are all for the most intense exposure scenarios -- small birds or mammals feeding exclusively on small grass."

Response: EPA has answered Valent's concerns in the Terrestrial Exposure section above.

Comment: "The granular formulation of acephate is based on ammonium sulfate. The formulation is hydroscopic and soluble in water. The small granules are short lived in the field, and being inorganic salt fertilizer, are distasteful to birds.

Response: EPA is not aware of taste avoidance of birds in regards to inorganic salt fertilizer. If registrant has data to show avoidance of birds to inorganic salt fertilizer, the Agency would be willing to reconsider its assumption that birds do not avoid these granules. In addition, the granules are not necessary short lived in the field since they have polymers that hold the ammonium sulfate together as a slow release fertilizer.

Comment: "Aquatic/Marine: With reduced methamidophos concentrations, acute and chronic exposure to aquatic and marine fish, arthropods and other invertebrates show RQ values that only exceed levels of concern for endangered species and restricted use for acute toxicity to the aquatic arthropod, *Daphnia*. Given the conservative nature of the EEC values used, these LOQ values, all less than one, do not indicate high risk."

Response: The calculated RQ for aquatic invertebrates from exposure to the methamidophos degradate exceeds the level of concern for high acute risk (0.5). Please note that the changes in the EECs resulting from the assumption of 25% conversion (rather than 77%) do not qualitatively affect the conclusions of the assessment of the risk to nontarget aquatic animals, i.e., for most uses the LOC for acute risk to aquatic invertebrates are exceeded. There are no exceedances for freshwater fish, mysid shrimp, or estuarine fish.

Comment: Valent agrees that some studies show deleterious effects, such as eggshell quality, and incubation and brood rearing behavior, from short-term chemical exposure. But for the purpose of this ACEPHATE risk assessment, Valent believes it is most appropriate to consider toxicology studies designed to evaluate the effects of acephate. There is no evidence that short-term, dietary exposure to acephate educes chronic effects.

Response: EPA disagrees and maintains that the lack of data for short-term chronic effects does not minimize chronic risk from the use of acephate. The criteria for avian reproductive studies were developed when the test was primarily used to determine effects of organochlorine pesticides and other persistent chemicals and reflect the concern for pesticides with chronic exposure patterns. The criteria would not necessary trigger a test for pesticides that pose risk of adverse reproductive effects from short term exposure. Several pesticides have been shown to reduce egg production within days after initiation of dietary exposure (Bennett et al 1991, Bennett and Bennett, 1991). Effects of eggshell quality (Bennett and Bennett, 1990, Haegele and Tucker, 1974) and incubation and brood rearing behavior (Bennett et al, 1991, Brewer et al., 1988, Busby et al.,1990) have also resulted from short-term pesticide exposures. Therefore, for purposes of this risk assessment of acephate and methamidophos, the amount of time birds can be exposed to acephate or methamidophos after initial chemical exposure that will result in chronic effects can be as little as a day.

Risk to Terrestrial Ecosystems - Birds -Chronic Risk

Comment: Valent states that "the chronic risk assessment assumes that birds remain within an acephate treated field for a long time. In the guideline avian reproduction studies, mallards and quail were fed acephate fortified diets for 10 weeks prior to egg laying and throughout the egg laying period. It is unreasonable to expect migrating birds to remain in one field for 16 weeks, the length of the guideline reproduction study. We are unaware of data demonstrating acephate-related, chronic effects from short term exposure."

Response: EPA has responded to this in the section discussing eggshell thinning above.

Risk to Terrestrial Ecosystems - Chronic Risk to Mammals

Comment: Valent has stated that in the chronic (rat reproduction) study cited by the Agency, rats were fed acephate fortified diets from adolescence, during mating, and throughout gestation/lactation, and into the next generation. The total exposure period was approximately 150 days for each generation. In the environment, both acephate and methamidophos degrade rapidly. Rapid degradation to nontoxic compounds precludes exposure times in the field approaching those required to reduce pup viability in the guideline reproduction study.

Response: The Agency maintains that there are data to show that some of the organophosphate and organochlorine pesticides do cause chronic effects on birds during a short time frame. Since there are no data to preclude risk to birds from the use of acephate, high chronic risk to birds from a short period of exposure is recognized. On the basis of the data from birds, the Agency has concerns that mammals also can be chronically affected from short term exposure. There are no available data to show that mammals can not be chronically affected by organophosphate pesticides from short term exposure. Until the Agency has data that shows that mammals will not be chronically affected from short term exposure to acephate, the Agency will have to assume that short term exposure may chronically affect mammals. Based on the data available to EPA and the

rate of application, the Agency has identified chronic risk to mammals.

Risk to Aquatic Ecosystems - Freshwater Environments

Comment: Valent says “the Agency cites mussel die-offs in North Carolina in August as evidence that acephate use MAY cause significant mortalities. Valent reiterates that NO acephate residues were found in mussel tissue and it is highly unlikely that acephate was the causative agent. Low water flow and high temperatures, both conducive to low oxygen concentration, are more likely to have cause (sic) the die-off.”

Response: The Agency never said that acephate was identified as the causative agent of the mussel die-offs, but only stated that acephate can cause such die-offs during periods of warm temperatures. The authors of the scientific article cite the high amounts of ChE inhibition measured in the mussels during the die-offs in North Carolina as evidence that organophosphates or carbamates may be responsible although no pesticide residues were measured. ChE inhibition is a characteristic of organophosphate poisoning. The authors later took some mussels and were able to duplicate the die-offs and measure high levels of ChE inhibition with the introduction of acephate. Although acephate residues were not found, the study did determine that acephate can cause mussel die-offs during warm periods. Later in another study the authors used acephate to show that acephate can cause adverse effects to mussels.

Part II: Non-Chemical-Specific Comments and Responses

Non-chemical-specific comments were received from the California Celery Research Advisory Board, the Cranberry Institute and Valent U.S.A. Corporation.

1. Comments from the California Celery Research Advisory Board

Run-Off/Drift Models

Comment: Bob Gray commented that EPA "models for runoff/drift substantially overestimate the potential contamination of surface waters, especially when compared to measured values in surface waters. The agency should make more of an effort to compare their calculated exposures with actual measured values from the field."

Response: In the presentation to the Science Advisory Panel in May, 1999 (presentation title: *Proposed Methods for Determining Watershed-derived Percent Crop Areas and Considerations for Applying Crop Area Adjustments to Surface Water Screening Models*), it was demonstrated in a comparison of modeled values to monitoring data that PRZM-EXAMS does not consistently overestimate concentrations of pesticide residues in surface waters. The commenter is referred to the OPP web site (www.epa.gov/scipoly/sap) for the full text of the presentation.

Chronic Exposure Estimates

Comment: The California Celery Research Advisory Board has commented that it is not clear why the calculations for chronic exposure to wildlife use the same exposure values as for acute exposures. There are no circumstances where wildlife would be continuously exposed to the maximum exposure amounts.

Response: EPA's current approach for screening for possible reproduction risks to birds allows for the use of a short time period-based Estimated Environmental Concentration (EEC). Sturkie (1986) summarizes the physical and biochemical events preceding and contemporary with significant reproduction events in birds. This information suggests that there are a number of processes important to the onset of follicular formation, ovulation, eggshell formation, and spermatogenesis that could be open to interference by xenobiotics, and that the possibility for short-term disruptions of these processes could have profound implications for the overall reproduction process. Indeed, the development of the ovarian follicle, ovulation, and egg laying may only span two or fewer weeks and all subsequent effects observed in embryos and hatchlings may be the result of exposure during this short phase, or during any point in the overall life cycle critical to reproduction. Certainly, the work of Bennet and Bennet (1990) with methyl parathion suggests that reproduction impairment can occur with some pesticides after exposure periods much shorter (only eight days) than the currently employed testing guideline but at comparable dietary concentrations.

For most pesticides, the toxicological data are not sufficient to characterize the duration of exposure required to induce reproduction impairment. The current reproduction tests used to satisfy OPP data requirements maximize the sensitivity of gross measurements of reproduction impairment but do not allow for discrimination between effects expressed from short-term exposure and effects requiring long-term exposure. The tests do not allow for the identification of critical exposure timing.

If EPA's current screen suggests that exposure may pose reproduction risk, further discussion and characterization of the potential risk is included. This discussion may take into account information on the use and environmental fate of the chemical, and environmental conditions that affect exposure levels and exposure duration. This discussion may also characterize the reproductive and sub-lethal risk in context of the range of possible exposure levels on food items and the distribution of possible exposure levels across food items, under various conditions, and over time.

In general, the short-term EEC will be used for the initial screen unless scientifically sound toxicity data are available that clearly delimit the length of time required to cause reproduction effects and identify the critical period in the life cycle.

2. Comments from the Cranberry Institute

Chemigation Systems

Comment: Jeff Downing provided information on the use of chemigation systems on cranberry farms as it impacts applicator mixer/loader occupational exposure.

Response: Because no specific comments were made concerning the environmental fate or ecotoxicology of acephate, EPA has no response. However, the Agency used this information to refine the acreage treated during chemigation on cranberry farms in its revised Occupational Exposure and Risk Assessment. The acreage changes should be addressed during label modification. Also, the Agency is requesting additional information from the registrant regarding the application methods, equipment, cultural practices and exposure monitoring data for acephate treatment of cranberries.

3. Comments from Valent U.S.A Corporation

Nongranular Applications

Comment: "The Table, Estimated Environmental Concentrations on Avian and Mammalian Food Items (ppm) Following a Single Application at 1 lb ai/A, gives Kenaga nomograph and Fletcher modified theoretical concentrations on various food items. Both references list fruits and pods and seeds as separate items.

"The Kenaga nomograph values for fruits and pods and seeds are 7 and 12 ppm, respectively; the Fletcher values are 4 and 5.4 ppm, respectively. Neither reference predicts concentrations in either small or large insects."

Response: In 1986, EPA established the Standard Evaluation Procedure for ecological Risk Assessment (EPA-540/9-85-001). This procedure used the Hoerger and Kenaga (1972) data for residues on forage as an estimate for small insects. This decision is supported by the position of Kenega (1973), which states: "Initial residues on insects are probably in the same order as those on plants of similar surface area to mass ratios..... Most of the factors which affect the decline of residues on plant surfaces are also operative for insect surfaces and so inert residues may be estimated on the basis of insect species having a surface to mass ratio similar to those of equivalent plant type...."

Kenega (1973) goes on to develop categories of residues with groupings of residue equivalency that include dense foliage and insects together as well as seeds, fruit, and large insects together. Kenega's (1973) findings have been applied to the data summarized by Fletcher et al. (1994), yielding the present Ecological Risk Assessment assumptions of residue equivalence between broadleaf/forage plants and small insects as well as between fruits, pods, seeds, and large insects.

EPA is open to consideration of any technically valid and statistically robust studies of residues on avian food items.

References

Fletcher, J.S., J.E. Nellessen, and T.G. Pfleeger. Literature review and evaluation of the EPA food-chain (Kenega) nomogram, an instrument for estimating pesticide residues on plants. Environmental Toxicology and Chemistry 13;1383-1391.

Hoerger, F. and E.E. Kenega. Pesticide residues on plants: Correlation of representative data as a basis for estimation of their magnitude in the environment. Environmental Quality and Safety 1:9-27.

Kenega, E.E. 1973. Factors to be considered in the evaluation of the toxicity of pesticides to birds in their environment. Environmental Quality and Safety 2:166-181.

Calculation of Ave. EEC and days EEC is less than NOAEC

Comment: Valent says that the Agency should explain more clearly how the values in "Ave. EEC during Application" and "days EEC is less than NOAEC" were calculated. Valent further notes that acute and chronic values were based on maximum EEC (Kenaga) while the "days EEC is less than NOAEC" uses the peak mean EEC (Fletcher) scenario. All of the values in the columns should have the same basis.

Response: Upon further reflection, EPA believes that the "Ave. EEC during Application" and "days EEC is less than NOAEC" columns of the bird and mammal RQ tables in the Ecological Risk Assessment do not provide any additional useful information. Therefore, to make the document more uniform with other Ecological Risk Assessments, those two columns will be removed.

Risk to Terrestrial Ecosystems - Mammals - Liquid Formulations - Acute Risk

Comment: Valent states that "Depressed ChE is an indicator of exposure to organophosphate insecticides, including acephate. There is no evidence to support the contention that mild (15%) ChE depression causes adverse affects, even in small mammals (squirrels and deer mice)."

Response: EPA will delete the statement indicated in quotes above from the Ecological Risk Assessment.